United States District Court
District of Massachusetts

Hull Leavitt,	)	
	)	
Plaintiff,	)	
	)	
v.	)	
	)	**Civil Action No.**
Alnylam Pharmaceuticals, Inc. et al.	)	**18-12433-NMG**
	)	
Defendants.	)	
	)	

MEMORANDUM & ORDER

GORTON, J.

This is a putative securities fraud class action brought by lead plaintiff Tunc Toker ("Toker") on behalf of himself and other similarly situated investors against Alnylam Pharmaceuticals, Inc. ("Alnylam") and certain Alnylam executives ("the Individual Defendants") (collectively "defendants"). Toker has alleged that defendants violated Sections 10(b) and 20(a) of the Securities Exchange Act of 1934 ("the Exchange Act"), 15 U.S.C. §§ 78j(b) & 78t(a), and Rule 10b-5 by making false and/or misleading statements during the Class Period regarding the efficacy and marketability of "Patisiran", a new drug designed to treat hereditary transthyretin-mediated amyloidosis ("hATTR amyloidosis").

In March, 2020, this Court dismissed the first amended complaint ("FAC") for failure to state a claim. Pending before the Court now is plaintiff's motion for leave to file a second amended complaint ("SAC") (Docket No. 75). Because this Court finds that the filing of the SAC would be futile, the motion will be denied.

I. Background

A. Facts

The facts of this case have been previously recited by this Court. See Docket Nos. 40 & 70. In brief, hATTR amyloidosis is a gene mutation which causes a potentially harmful build-up of certain proteins in the body's nerves and organs and manifests in two ways: damage affecting the nerves (polyneuropathy) and damage impacting the heart (cardiomyopathy). Patients often exhibit both manifestations.

In 2013, Alnylam initiated a Phase 3 clinical trial, APOLLO III, designed primarily to evaluate the efficacy and safety of Patisiran for treating polyneuropathy in hATTR amyloidosis patients. Although the primary study endpoints were polyneuropathy-related, approximately 56% of the study population exhibited both polyneuropathy and cardiomyopathy ("the cardiac sub-population") and the trial had many secondary and exploratory endpoints which sought to measure the efficacy

of Patisiran for a variety of non-neurological clinical parameters, including cardiac health.

Alnylam was simultaneously conducting a clinical trial for "Revusarin", a drug designed specifically to treat hATTR amyloidosis patients with cardiomyopathy, until that trial was halted in October, 2016, due to safety concerns. The APOLLO III trial continued, however, and was completed in September, 2017. Thereafter, Alnylam executives reviewed the APOLLO III data and as of November, 2017 began, for the first time, to express optimism that APOLLO III supported broad-label FDA approval for Patisiran (i.e., both polyneuropathy and cardiomyopathy indications). At that time, there were no FDA-approved drugs which treated hATTR amyloidosis, in any form, and two other pharmaceutical companies, Ionis and Pfizer, were racing against Alnylam to be the first to bring such a drug to the market.

In December, 2017, Alnylam submitted to the FDA a new drug application ("NDA") and marketing authorization application for Patisiran and continued to make public statements forecasting a high likelihood that, based on APOLLO III, the drug would be approved to treat all manifestations of hATTR amyloidosis, i.e., both polyneuropathy and cardiomyopathy ("broad-label approval"). In August, 2018, however, the FDA approved Patisiran for the treatment of only polyneuropathy manifestations of hATTR amyloidosis. Around the same time and based on the same data,

the European Medicines Agency ("the EMA") approved the drug for all manifestations of the disease (in patients with polyneuropathy) and authorized inclusion of cardiac data on the drug label.

A month later, the FDA released a report ("the Final Report") discussing its review of Patisiran which several analysts characterized as critical of Alnylam for having provided insufficient cardiac efficacy data to support a cardiomyopathy indication. Soon thereafter, Alnylam's stock price fell and this lawsuit was filed. Plaintiff alleges that between September 20, 2017, and September 12, 2018 ("the Class Period"), defendants misleadingly stated to investors that APOLLO III data supported a dual treatment indication for Patisiran, namely, polyneuropathy and cardiomyopathy, thereby causing the company's stock price to become artificially inflated and permitting the defendants to reap a profit of $66 million from insider stock sales. When the alleged misrepresentations were disclosed to the public, plaintiff asserts, the stock price fell precipitously causing investors to suffer economic loss.

B. Procedural History

In September, 2018, Carol Leavitt filed this action in the United States District Court for the Southern District of New York and it was transferred to this Court in late November,

2018. In May, 2019, this Court appointed Tunk Toker as lead plaintiff and in July, 2019, he filed the FAC.

In March, 2020, this Court dismissed the FAC (the "Dismissal Order"), finding generally that 1) plaintiff did not plead specific facts demonstrating that the defendants either knew broad label FDA approval for Patisiran was "impossible" or otherwise fraudulently mischaracterized the purpose or potential of APOLLO III and 2) plaintiff's insider-trading-based allegations of scienter were inadequate.

Plaintiff filed the instant motion for leave to file the SAC in June, 2020, and has attached thereto a proposed SAC. Defendants object to the amendments exclusively on the ground that they fail to establish a strong inference of scienter.

C. New Allegations of Scienter

Plaintiff submits that the proposed SAC responds to the deficiencies noted by this Court in its Dismissal Order and, now, establishes a strong inference of scienter. First, he explains that the SAC has removed misstatements relating to whether the FDA would approve any cardiac data on the Patisiran label and, instead,

> narrowly focuses on Alnylam's ability to secure a dual indication for patisiran that would, for example, allow for treatment of patients with pure cardiac manifestations of hATTR Amyloidosis based on APOLLO III.

Second, the SAC adds the opinion of Dr. Darren Scheer, a purported regulatory expert, which plaintiff contends establishes that such dual indication approval was "radically implausible" (rather than impossible) because 1) APOLLO III was never designed to test the efficacy of Patisiran for cardiomyopathy hATTR amyloidosis patients, 2) the study had no primary or secondary cardiac endpoints "which are critical to support an FDA indication" and 3) defendants provided no cardiac efficacy data to the FDA. Based on that opinion, the SAC declares that defendants, as "expert medical doctors, PhDs and veteran pharmaceutical executives", knew or recklessly disregarded that APOLLO III did not support a cardiomyopathic indication but, nonetheless, told the market that they

> anticipate a label that patisiran will be indicated for treatment of [h]ATTR amyloidosis, ***period, full stop***.

(emphasis in original).

Defendants respond that the claims of scienter in the proposed SAC are just as weak as they were in the FAC. The SAC provides no direct allegations of scienter and inadequate circumstantial claims that defendants "must have known" that their statements were misleading because of their education and experience.

With respect to whether defendants knew that dual indication approval was "radically implausible", moreover,

defendants contend that nothing in the SAC suggests that either Dr. Scheer or the FDA expressed their skepticism relating to APOLLO III's cardiac data with the defendants during the Class Period. Furthermore, defendants aver that the EMA used that same data to approve Patisiran for both manifestations of hATTR amyloidosis when used by polyneuropathy patients and allowed the cardiac data to be included on the drug label.

Finally, defendants submit that the allegations of scienter in the SAC "amount to nothing more than a disagreement between Alnylam and the FDA". They argue that the more compelling inference is that

> the FDA, in its unilateral authority, approved a more narrow label and more narrow indication, based on its own review and interpretation of the APOLLO data, than Defendants anticipated and honestly believed was warranted, based on their interpretation of the [same] data.

II. Motion for Leave to Amend

A. Legal Standard

A party may amend his pleading by leave of the court, which should be "freely give[n] . . . when justice so requires". Fed. R. Civ. P. 15(a)(1); Holbrook v. Boston Scientific Corp., No. 20-10671, 2020 WL 5540544, at *1 (D. Mass. Sept. 16, 2020). Rule 15(a) gives courts wide discretion in deciding whether to allow or deny leave to amend. U.S. ex rel. Gagne v. City of Worcester, 565 F.3d 40, 48 (1st Cir. 2009). A court acts within that discretion if it denies leave for reasons of, inter alia,

undue delay in filing the motion, repeated failure to cure deficiencies, undue prejudice to the opposing party or futility of amendment. Id.

A proposed amendment is futile if it "does not plead enough to make out a plausible claim for relief". HSBC Reality Credit Corp. v. O'Neill, 745 F.3d 564, 578 (1st Cir. 2014). Futility thus applies "the same standard of legal sufficiency as applies to a Rule 12(b)(6) motion." Glassman v. Computervision Corp., 90 F.3 617, 623 (1st Cir. 1996). To survive such a motion, a complaint must contain "sufficient factual matter" to state a claim for relief that is actionable as a matter of law and "plausible on its face." Ashcroft v. Iqbal, 556 U.S. 662, 667 (2009) (quoting Bell Atl. Corp. v. Twombly, 550 U.S. 544, 570 (2007)).

A claim is facially plausible if, after accepting as true all non-conclusory factual allegations, the court can draw the reasonable inference that the defendant is liable for the misconduct alleged. Ocasio-Hernandez v. Fortuno-Burset, 640 F.3d 1, 12 (1st Cir. 2011). A court may not disregard properly pled factual allegations even if actual proof of those facts is improbable. Id. Rather, the relevant inquiry focuses on the reasonableness of the inference of liability that the plaintiff is asking the court to draw. Id. at 13. When rendering that determination, a court may not look beyond the facts alleged in

the complaint, documents incorporated by reference therein and facts susceptible to judicial notice. Haley v. City of Boston, 657 F.3d 39, 46 (1st Cir. 2011).

Actions involving securities fraud claims must also satisfy the heightened pleading standards imposed by Fed. R. Civ. P. 9(b) and the PSLRA. See Kader v. Sarepta Therapeutics, Inc., 2017 WL 72396 (D. Mass. Jan. 6, 2017).

B. Application

1. Section 10(b) and Rule 10b-5

To state a claim for securities fraud pursuant to Section 10(b) of the Exchange Act and Rule 10b-5, a plaintiff must adequately plead, inter alia, scienter. Corban v. Sarepta Therapeutics, Inc., 868 F.3d 31, 37 (1st Cir. 2017). Scienter is a "mental state embracing intent to deceive, manipulate or defraud". ACA Fin. Guar. Corp. v. Advest, Inc., 512 F.3d 46, 58 (1st Cir. 2008) (quoting Ernst & Ernst v. Hochfelder, 425 U.S. 185, 193 n.12 (1976)). It requires a showing that defendants either "consciously intended to defraud, or that they acted with a high degree of recklessness". Id. (quoting Aldridge v. A.T. Cross Corp. 284 F.3d 72, 82 (1st Cir. 2002)).

That degree of recklessness involves "a highly unreasonable omission" and

> not merely simple, or even inexcusable, negligence, but an extreme departure from the standards of ordinary care, and which presents a danger of misleading buyers and sellers

> that is either known to the defendant or so obvious that the actor must have been aware of it.

Brennan v. Zafgen, Inc., 853 F.3d 606, 613 (1st Cir. 2017).

Under the PSLRA, plaintiff must "state with particularity facts giving rise to a strong inference of scienter". 15 U.S.C. § 78u-4(b)(2) (emphasis added). Those allegations "should be evaluated with reference to the complaint as a whole rather than to piecemeal allegations". ACA Fin. Guar. Corp., 512 F.3d at 59.

The Supreme Court of the United States has instructed that, to qualify as "strong",

> an inference of scienter must be more than merely plausible or reasonable—it must be cogent and at least as compelling as any opposing inference of nonfraudulent intent.

Tellabs, Inc. v. Makor Issues & Rights, Ltd, 551 U.S. 308, 314 (2007). Such a showing is often supported by direct evidence, including admissions, internal records or other "smoking guns" suggesting that the defendants "were aware that they were withholding vital information or at least were warned by others that this was so". In re Boston Sci. Corp. Sec. Litig., 686 F.3d 21, 31 (1st Cir. 2012); see Tellabs, 551 U.S. at 324.

"When there are equally strong inferences for and against scienter, the draw is awarded to the plaintiff". City of Dearborn Heights Act 345 Police & Fire Ret. Sys. v. Waters Corp., 632 F.3d 751, 757 (1st Cir. 2011).

Here, plaintiff maintains that he met the PSLRA's requirements for pleading scienter by alleging that 1) defendants, as highly educated pharmaceutical executives, knew or recklessly disregarded the fact that the design of APOLLO III rendered FDA approval of a dual treatment indication for Patisiran "radically implausible" and 2) defendants had a motive to commit securities fraud once their cardiomyopathy-focused drug, Revusiran, failed in order to "be the first to market an FDA-approved drug to treat hATTR amyloidosis" and to "reap tens of millions of dollars in insider sales proceeds".

i. Knowledge or Recklessness

Even assuming, arguendo, that defendants' forecasts of FDA approval of a broad label for Patisiran were materially misleading, this Court concludes that the factual allegations in the proposed SAC fail to give rise to a strong inference of scienter. Nothing in the SAC insinuates that defendants knew or recklessly disregarded that full approval was "radically implausible". There is no direct claim of such knowledge nor the prospect of adequate circumstantial evidence.

Missing from the SAC is any allegation of a "smoking gun" or contention that Dr. Scheer (plaintiff's "regulatory expert") or others shared with defendants, during the Class Period, the opinion that APOLLO III could not support broad-label FDA approval. The proffered opinion of Dr. Scheer, moreover, does

not even assess the likelihood of broad-label approval but is, instead, limited to the likelihood that the FDA would grant approval for only a cardiomyopathy indication for Patisiran. Meanwhile, the purportedly misleading statements of the defendants anticipate a broad label and not an exclusively cardiomyopathy-related indication for the drug, explaining that 1) hATTR amyloidosis can be considered one disease, 2) the APOLLO III results were strong across the board and 3) the study, therefore, supports approval for Patisiran to treat the disease in all of its forms.

Also missing is any allegation that the FDA, at any time prior to the release of its Final Report in September, 2018, expressed to defendants its disapproval of APOLLO III's cardiac data. Just because the Individual Defendants are highly educated pharmaceutical executives familiar with clinical trial design and FDA practice does not mean, ipso facto, they "must have known" that the design of APOLLO III rendered dual indication approval for Patisiran radically implausible. See, e.g., Coyne v. Metabolix, Inc., 943 F. Supp. 2d 259, 272 (D. Mass. 2013) ("It is also well established that scienter allegations based solely on a defendant's high-ranking position in the company are not sufficient."); Bd. of Tr. Of City of Ft. Lauderdale Gen. Emps.' Ret. Sys. v. Mechel OAO, 811 F. Supp. 2d 853, 873 (S.D.N.Y. 2011) ("[G]eneralized allegations about the

Individual Defendants' educational backgrounds and extensive experience . . . do not raise an inference [of scienter]." (internal quotation marks omitted)).

Furthermore, as this Court stated in its Dismissal Order, the study design and its corresponding statistical analysis contradict plaintiff's contention that APOLLO III failed to evaluate efficacy for cardiomyopathy or hATTR amyloidosis more generally.[1] Although APOLLO III was intended primarily to evaluate Patisiran's efficacy and safety with respect to patients with polyneuropathy, a cardiac sub-population comprised over 50% of the study participants. The study also contained a number of measures designed to test various non-neurological metrics, including cardiac health, which produced positive results. Hence, in the November, 2017, FDA meeting minutes, the relevant Division suggested to Alnylam that its

> NDA submission should include mutation subset analyses in order to support the generalizability of the efficacy results [for Patisiran] to a broader population of patients with mutations that were not represented in the trial.[2]

---

[1] The Court may, in its discretion, take judicial notice of FDA documents. Kader, 2017 WL 72396, at *2 n.3.

[2] See also, Food and Drug Administration, Indications and Usage Section of Labeling for Human Prescription Drug and Biological Products – Content and Format Guidance for Industry (July, 2018), https://www.fda.gov/files/drugs/published/Indications-and-Usage-Section-of-Labeling-for-Human-Prescription-Drug-and-Biological-Products-%E2%80%94-Content-and-Format-Guidance-for-Industry.pdf (draft) ("In some cases, FDA's expert reviewers may fairly and responsibly conclude, based on their scientific training and experience, that the available evidence supports

Moreover, in 2019, the EMA approved Patisiran to treat both neuropathy and cardiomyopathy in polyneuropathy hATTR amyloidosis patients and allowed the inclusion of APOLLO III cardiac efficacy data in the label.

FDA approval for dual treatment indication may have been significantly less likely than approval for exclusively polyneuropathy but the record indicates that defendants could have reasonably believed that, given the positive APOLLO III results, a broad label was plausible. Thus, as defendants suggest, the more compelling inference is that the FDA merely disagreed with defendants' proposed scope for Patisiran and approved a more narrow label and indication than defendants anticipated and fairly believed was warranted. See Harrington v. Tetraphase Pharm. Inc., No. 16-cv-10133, 2017 WL 1946305, at *5 (D. Mass. May 9, 2017) ("[C]ourts have been clear that scientific opinions are just that: opinions.").

ii. Motive and Opportunity

Plaintiff also re-asserts in the SAC various allegations as to defendants' motive to commit securities fraud. Although a strong inference of scienter may be established by combining various facts and circumstances indicating fraudulent intent,

---

approval of an indication that is broader or narrower in scope than the precise population studied.").

including "motive and opportunity", Aldridge, at 284 F.3d at 82, plaintiff's allegations of motive in this case fall short.

For instance, plaintiff contends that defendants were motivated to mislead the public that APOLLO III supported a dual polyneuropathy/cardiomyopathy indication for Patisiran, in part, because Revusiran (the cardiomyopathy-focused drug) had failed and Alnylam wanted to beat Pfizer and Ionis to market with the first FDA-approved hATTR amyloidosis treatment. That contention is, however, undermined by chronology. Specifically, Revusiran "failed" in October, 2016, but defendants did not begin forecasting broad-label FDA approval for Patisiran until the fall of 2017, after they had received and reviewed the APOLLO III data. That timing presents the more plausible inference that positive APOLLO III results, not the failure of Revusiran, motivated defendants' statements.

With respect to the insider trading allegations, they remain largely unaltered from those in the FAC which this Court previously dismissed. Still relevant is the fact that one of the Individual Defendants traded no Alnylam stock during the Class Period and another acquired more stock than she sold. See Fire & Police Pension Ass'n of Colorado v. Abiomed, Inc., 778 F.3d 228, 246 (1st Cir. 2015) (noting that a defendant who increases her holdings during the Class Period negates an inference of scienter); see also Acito v. IMCERA Grp., Inc., 47

F.3d 47, 54 (2d Cir. 1995) ("The fact that the other defendants did not sell their shares during the relevant class period undermines plaintiffs' claim that defendants delayed notifying the public so that they could sell their stock at a huge profit." (internal quotation marks and citations omitted)).

Even viewing the allegations of motive in light of the other scienter allegations, plaintiff has failed to aver a strong inference of scienter. See Fire & Police Pension Ass'n of Colorado, 778 F.3d at 246 ("For stock sales by corporate officials to bolster an inference of scienter, the trading must be, at a minimum, … unusual, well beyond the normal patterns of trading by those defendants" (internal quotation marks and citation omitted)). Accordingly, the amendment with respect to plaintiff's Section 10(b) and Rule 10b-5 claim is futile for lack of scienter and his motion to amend will, therefore, be denied.

2. Section 20(a)

The SAC also asserts a claim for control person liability pursuant to Section 20(a) of the Exchange Act against the individual defendants. Section 20(a) imposes joint and several liability on any person who, "directly or indirectly, controls any person liable" under Section 10(b) and Rule 10b-5. 15 U.S.C. § 78t(a). Because the SAC fails to allege an underlying violation of the federal securities laws, the amendment with

respect to plaintiff's Section 20(a) claim is also futile. See Greebel, 194 F3d at 207.

3. Dismissal with Prejudice

Having found that plaintiff, for the second time, fails to state actionable claims for securities fraud and control person liability, the Court will deny plaintiff's motion to amend with prejudice.

ORDER

For the foregoing reasons, plaintiff's motion for leave to amend (Docket No. 75) is **DENIED with prejudice.**

So ordered.

/s/ Nathaniel M. Gorton
Nathaniel M. Gorton
United States District Judge

Dated March 12, 2021